II. REMARKS

Upon entry of the present Amendment, claims 44-47, 54-56 and 60-62 will be pending. Claim 44 has been amended. Support for this amendment can be found throughout the specification, and in particular, on page 11, lines 6 to 25, and on page 12, lines 24 to 29. Accordingly, no new matter is introduced. Reconsideration of the rejections raised in the Final Office Action dated April 8, 2002 is respectfully requested in light of the foregoing amendments and remarks that follow.

The Examiner Interview

Applicants would like to thank the Examiner for conducting the interview which took place on June 17, 2002. As suggested by the Examiner, the claims have been amended to exclude sample filtering, and the unexpected results achieved with the claimed invention are discussed herein.

Discussion regarding the subject invention

Claim 44 has been amended herein for clarity and now recites a five step method, with the steps of obtaining a sample, grinding the sample, contacting the sample with the liquid permeable support, allowing the liquid to vertically flow through the support and detecting the presence of analyte. Claim 44 also now recites the preferred "dipstick" assay format, which involves vertical flow, as opposed to a lateral flow assay. In addition, claim 44 now recites the preferred "dipstick" construction, which includes a sample pad, at least one conjugate pad and an absorbent pad, in this order. Also claimed is the absence of a filter to remove cellular debris or particulate matter.

Discussion regarding unexpected results

Applicants have unexpectedly found that such an assay format (i.e. vertical flow) and dipstick construction allows unpure samples containing arthropod debris, which includes both cellular debris and particulate matter, to be used without requiring filtering or a sample purification step, since the arthropod debris settles to the bottom and does not flow up the liquid

permeable support and interfere with interpretation of test results. For example, since the dipstick includes an absorbent pad to facilitate liquid flow through the liquid permeable support, the flow rate is faster than it would be without an absorbent pad, which helps larger particles that have a slower flow rate remain outside the conjugate pad where they might interfere with interpretation of the test results. As such, the assay can be performed in 15 minutes. See Exhibit A attached hereto, which is the package insert included with the claimed assay that is currently on the market. Thus, while the preferred lateral flow device includes a filter, the vertical flow device unexpectedly does not need one.

Rejection under 35 U.S.C. § 103

Claim 44-46, 54-56 and 60-62 were rejected over Oprandy et al. ((1990) J. Clin. Microbiol. 28(8): 1701-03) ("Oprandy") in view of Huang et al. (US Patent No. 5,712,172) ("Huang").

The Primary Reference - Oprandy

Oprandy relates to a dot-blot immunobinding assay for detecting arthropod agents. Oprandy proposes that analyte obtained from homogenized mosquitoes can be tested through a multiple step process. This process entails the steps of purifying the sample through a premembrane filter, binding a spot of solubilized antigen to a high protein binding capacity membrane, then applying monoclonal antibody to the bound antigen. Oprandy does not teach a permeable support which facilitates separation of arthropod artifacts from analyte through capillary flow or diffusion. This reference also does not teach an analyte-specific reagent immobilized onto the support over which the sample is allowed to become purified and then immobilized by a capture reagent adapted for capturing unbound analyte or an analyte-reagent complex. More importantly, Oprandy does not teach vertical flow of the liquid sample through the permeable support. Accordingly, Oprandy does not disclose either step (c) or step (d) of the presently claimed invention.

The Secondary Reference - Huang

The Examiner alleges that, while Oprandy does not teach a lateral flow device for the detection of the analyte, the Huang reference does. However, the claims as amended herein are now directed to vertical flow devices, i.e. "dipsticks", not lateral flow devices.

The Examiner reasons that it would be obvious to adapt the Oprandy method to a different assay format, such as an ELISA, since they both depend on antibody-antigen interactions.

Motivation to combine Oprandy and Huang

"In determining whether the invention as a whole would have been obvious under 35 U.S.C. 103, we must first delineate the invention as a whole. In delineating the invention as a whole, we look not only to the subject matter which is literally recited in the claim in question....but also to those properties of the subject matter which are inherent in the subject matter *and* are disclosed in the specification... Just as we look to a chemical and its properties when we examine the obviousness of a composition of matter claim, it is the invention *as a whole*, and not some part of it, which must be obvious under 35 U.S.C. 103." MPEP, Section 2141.02, quoting from *In re Antonie,* 559 F.2d 618, 620, 195 USPQ 6, 8 (CCPA 1977)(emphasis in original)(citations omitted).

The instant invention is a five step method that is adapted specifically for assaying arthropod borne analytes in samples that contain arthropod debris. As amended herein, the claims now require a particular dipstick construction which, unexpectedly, is very well suited for samples containing arthropod debris. In order to find Applicants' invention obvious, the Examiner must consider all five steps, and the dipstick construction, together. Oprandy fails to teach two of the five steps, and Huang is not even in the same field. Moreover, Oprandy does not teach or suggest a dipstick format. Applicants are aware of the widespread use of various different immunologic assay formats for performing immunoassays. However, Applicants' presently claimed five step method, when viewed as a whole, is not rendered obvious over individual references that teach some but not all of the steps, unless there is some motivation to combine the references to arrive at Applicants' claimed invention.

"[A] patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. This is part of the 'subject matter as a whole' which should always be considered in determining the obviousness of an invention under 35 U.S.C. § 103." MPEP, Section 2141.02, quoting from *In re Sponnoble,* 405 F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969). However, "discovery of the cause of a problem...does not always result in a patentable invention...[A] different situation

exists where the solution is obvious from prior art which contains the same solution for a similar problem.." MPEP, Section 2141.02, quoting from *In re Wiseman*, 596 F.2d 1019, 1022, 201 USPQ 658, 661 (CCPA 1979)(emphasis in original).

Applicants' invention solves a problem - the problem relates to the fact that arthropod-borne disease-carrying agents must first be removed from the arthropods before they can be assayed. And, cellular and arthropod debris in a sample can interfere with the interpretation of results. Applicants solved the problem by using a specific assay format that relies on gravity to keep the arthropod debris from interfering with the assay, and a specific dipstick construction that facilitates separation of debris from the analytes in the sample. Oprandy solved the same problem in a different way - Oprandy taught the use of a premembrane to eliminate "any coloration on the assay membrane from the arthropod material" (page 1703, first column). Although Applicants' solution to the problem may seem to be a simple one in hindsight, Applicants' invention is not obvious over Oprandy's teaching, unless the secondary references suggest Applicants' claimed solution to the problem embodied in steps (c) and (d). Respectfully, Applicants do not believe Oprandy makes any such suggestion.

Rattanarithikuln and Sithiprasasna

Regarding multiple analyte assays, the Examiner has cited Rattaharithikuln et al. (American Journal of Tropical Medicine(1996)) and Sithiprasasna et al. (Annals of Tropical Medicine and Parasitology ( )). However, neither of these two references disclose what is missing from Oprandy and Huang - namely, Applicants' steps (c) and (d). Accordingly, these references cannot render Applicants' claimed invention obvious either.

III. CONCLUSION

Applicants believe that this Preliminary Amendment addresses all of the rejections in the Final Office Action dated April 8, 2002 and places the case in condition for allowance.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 355742104100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: 7/2/02

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EXHIBIT A: MARKED-UP VERSION OF AMENDMENTS TO THE CLAIMS.

44. (Amended) A method for analyzing an arthropod sample for the presence of one or more analytes associated with an arthropod-carried agent that causes a disease in mammals, said method comprising the steps of:

(a) obtaining an arthropod sample suspected of containing arthropod-borne agents;

(b) grinding the sample in solution to expose an analyte associated with the arthropod-carried agent such that the sample contains a liquid phase and arthropod debris after grinding;

(c) contacting a liquid permeable support with the sample containing arthropod debris from step (b) and a detectable analyte-specific reagent that binds to the analyte to form an analyte - reagent complex[, wherein said support further comprises a capture reagent immobilized therein that binds to the analyte or the analyte-specific reagent or the analyte-specific reagent complex], wherein said support comprises, in order:

(i) a sample pad adapted for receipt of the sample;

(ii) at least one conjugate pad having immobilized thereto a capture reagent that binds to the analyte or the analyte-specific reagent or the analyte-specific reagent complex;

(iii) an absorbent pad adapted to facilitate vertical liquid flow along the liquid permeable support;

wherein the liquid permeable support does not include a filter to remove cellular debris or particulate matter;

(d) allowing the liquid phase to vertically move through the support by capillary flow or wicking until the analyte or the analyte-specific reagent or the analyte-specific reagent complex binds to the capture reagent; and

[(d)] (e) detecting the presence of the detectable analyte-specific reagent indicating the presence of the analyte in the sample.